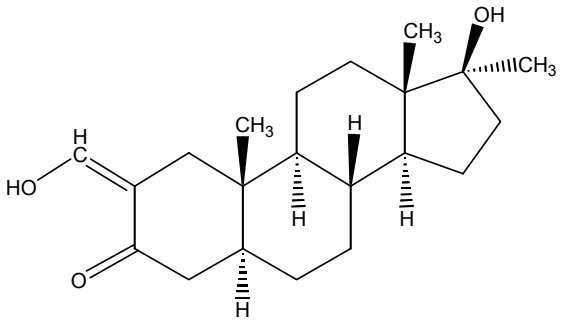
OXYMETHOLONE
CAS No. 434-07-1
First Listed in the *First Annual Report on Carcinogens*



CARCINOGENICITY

Oxymetholone is *reasonably anticipated to be a human carcinogen* based on limited evidence of carcinogenicity in humans (IARC 1977, 1982). Ten cases of liver tumors have been reported in patients with blood disorders treated for long periods with oxymetholone alone or in combination with other androgenic drugs; however, a causal relationship cannot be established. The increased risk of liver tumors could be related to hepatic damage known to be caused by oxymetholone. Alternatively, patients with congenital anemias may be at higher risk of developing these tumors, and this risk may become manifest during the extended survival resulting from oxymetholone treatment (IARC 1977, 1982).

No data were available to evaluate the carcinogenicity of oxymetholone in experimental animals at the time of the IARC monograph (IARC 1982). However, NTP (1999) recently evaluated the carcinogenicity to rats in gavage studies. NTP concluded that there was equivocal evidence of carcinogenic activity in male F344/N rats and clear evidence of carcinogenic activity of oxymetholone in female rats.

PROPERTIES

Oxymetholone is a white to creamy-white crystalline solid that is practically insoluble in water, soluble in ethanol, dioxane, and ether, and very soluble in chloroform. Oxymetholone is available in the United States as national formulary grade containing 97%-103% active ingredient on a dried basis, with a maximum of 3% foreign steroids or other impurities. It is stable in air (HSDB 2000).

USE

Oxymetholone is a synthetic anabolic-androgenic steroid hormone that is structurally related to the male hormone testosterone. Synthetic androgens are used to treat a variety of conditions including hypogonadism and delayed puberty. Androgens are also used to correct hereditary angioneurotic edema, manage carcinoma of the breast, promote a positive nitrogen balance following injury or surgery, and stimulate erythropoiesis. Considerable amounts of androgens are consumed by athletes in attempts to improve athletic performance. Oxymetholone is used to promote weight gain and counteract weakness and emaciation resulting from

debilitating diseases, such as advanced HIV infection, and after serious infections, burns, trauma, or surgery. It is marketed as a human prescription drug for the treatment of anemias caused by deficient red cell production. It has also been used in veterinary medicine as an anabolic steroid for small animals (IARC 1977, NTP 1999).

In 1972, the FDA permitted the use of oxymetholone to treat pituitary dwarfism and as an adjunctive therapy in osteoporosis pending further investigation. The FDA withdrew its approval for use of oxymetholone in the treatment of pituitary dwarfism in 1980 and in topically applied drug products for over-the-counter use in 1993 (21 CFR, Part 310). In 1983, the FDA allowed the continued use of oxymetholone for treatment of "certain anemias." Thus, the sanctioned uses of oxymetholone are limited (NTP 1999).

PRODUCTION

There is no evidence that oxymetholone has ever been produced commercially in the U.S., and no current production data were available for the compound. Chem Sources (2001) identified four current U.S. suppliers of oxymetholone. In 1977, U.S. sales of oxymetholone were estimated to be less than 44 lb annually (IARC 1977). No export or import data were available for oxymetholone; however, the U.S. imported approximately 35,000 lb of all anabolic agents and androgens in 2000 (ITA 2001).

EXPOSURE

The primary routes of potential human exposure to oxymetholone are ingestion and dermal contact. Health professionals such as pharmacists, physicians, and nurses may be potentially exposed to oxymetholone while dispensing or administering the substance. The risk of potential occupational exposure is low, since the compound is not produced in the U.S. The National Occupational Exposure Survey (1981-1983) indicated that an estimated 742 total workers, including 359 women, potentially were exposed to oxymetholone (NIOSH 1984).

Since the 1950s, increasing numbers of athletes have experimented with anabolic drugs in efforts to increase strength. Estimates in the 1980s indicated that 80% to 100% of national and international male bodybuilders, weightlifters, and participants in the shot put, discus, hammer, and javelin throws used anabolic steroids; football players and competitors in other sports used anabolic steroids to a lesser extent. Dosages used by athletes are often much higher than the normal endogenous testosterone production of 4 to 10 mg/day. Documented dosages range from 10 or 15 mg/day to 300 mg/day, with anecdotal reports of up to 2 g/day. Generally, a variety of injectable and oral steroids are taken at dosages that increase, peak, and then taper off prior to competitions and potential drug tests (NTP 1999).

REGULATIONS

Because oxymetholone is a pharmaceutical and is used in low quantities relative to other compounds, it is of little regulatory concern to EPA. There may be a small pollution problem relative to hospital wastes. Since there is no evidence of domestic manufacture, it is unlikely that EPA will investigate sources for possible regulation. FDA reduced the list of approved uses of oxymetholone in 1972 and again in 1983. Since 1977, FDA has required warning labels that indicate possible adverse effects of oxymetholone.

OSHA regulates oxymetholone under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table 142.

REFERENCES

Chem Sources. Chemical Sources International, Inc. http://www.chemsources.com, 2001.

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